

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application Serial No. 09/837,562)	
)	Group Art Unit: 1623
Filing Date: April 19, 2001)	
)	Examiner: McIntosh, Traviss C.
For: Composition And Method For)	
Normalizing Impaired Or)	Docket No: 12439.104US
Deteriorating Neurological Function)	(Formerly 12439.101B)
)	
Inventor: Edward Larry McCleary)	Attachment to Paper No. 11

DECLARATION OF EDWARD LARRY McCLEARY

I, Edward Larry McCleary, hereby declare:

1. I am a pediatric neurosurgeon. I am also involved in the business of nutritional supplements, which includes product development of nutritional supplement combinations for the brain and nervous system. All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true.

2. I have worked for over 25 years as a physician (MD). I am licensed to practice medicine and surgery (pediatric neurosurgery) in Colorado. I have published numerous professional papers and have made national and international presentations on various subjects pertaining to the field of pediatric neurosurgery. These topics span the fields of surgical technique, intra-operative real time imaging, spinal cord tumors, adoptive immuno-therapy for brain tumors, cerebral trauma, monitoring and therapy of intracranial hypertension, and metabolic aspects of neurosurgery. I have been involved in the training of medical, surgical, and neurosurgical residents and house staff. I have been an active member of the Childrens' Cancer Study Group (now Childrens' Oncology Group), and have participated in the design and implementation of cancer protocols. I have designed and helped conduct human clinical trials of nutritional supplement combinations for the treatment of various neurological conditions. I am currently writing a book based upon analytical methods used to evaluate the critical transitions in brain anatomy and function during

Serial No. 09/837,562

Declaration Of Edward Larry McCleary

Page 1 of 7

187551v1

development of a child's brain. This includes therapeutic applications of techniques based upon this analysis.

3. My formal training includes:

Dartmouth College, BA, 1971 (Rufus Choate Scholar)

Boston University, 1971-73, Theoretical Physics

State University of NY at Buffalo, MD, 1979 (AOA)

University of Minnesota Medical School, Surgical Residency 1980

Bellevue-New York University, Neurosurgery residency 1980-86

4. Following my neurosurgical training, I was a pediatric neurosurgeon at Denver Childrens' Hospital, where I was Acting Chief of Neurosurgery for 4 years. During the past decade, I have been involved in the use and development of nutritional supplement combinations for neurological/cognitive therapy.

5. I am the inventor named in the above-designated patent application (hereinafter, "the Application").

6. I have read the currently pending claims of the Application, as well as the Office Action dated July 28, 2003 (hereinafter, "the Office Action").

7. I submit this Declaration to present to the Examiner, in an authenticated manner, facts concerning the accuracy and interpretation of the specification (hereinafter, "the Specification") of the invention in the present Application, as well as concerning the Specification's relevance to the claims and to the statements of the Examiner in the Office Action.

8. There is no one-to-one correlation between treatment and cure. An impaired or a deteriorating neurological function can be treated without necessarily curing it. In common medical usage, the term "cure" connotes the eradication, reversal, or elimination of the primary disease-causing factor or factors. A cure does not necessarily constitute a good outcome. A treatment may, or may not, be related to the primary disease-causing factor that initiated a particular disease process. A treatment may also be directed at secondary causes of specific cellular impairment or failure. Embodiments in accordance with the invention treat such secondary causes,

Serial No. 09/837,562

Declaration Of Edward Larry McCleary

Page 2 of 7

187551v1

although the invention can also be applied to treat (not necessarily cure) a primary disease-causing factor. Such treatment considerations arise constantly in the daily practice of medicine and relate to the depth of understanding of the disease process, as well as to how an individual reacts to any specific disease process.

9. An example that serves to illustrate these concepts is a patient with meningitis. The primary disease-causing factor of meningitis is an infection. The complete elimination of the infection constitutes a cure. The administration of appropriate antibiotics typically cures meningitis. With the help of the body's immune system, antibiotics eradicate the infection. The cure of meningitis through elimination of the infection might, nevertheless, leave the patient in a state of impaired or deteriorating neurological function. Meningitis might be accompanied by seizures, stroke-like symptoms, cerebral edema, vascular thrombosis, or other associated causes of impaired or deteriorating neurological function. Any one these accompanying conditions may lead to impaired or deteriorating neurological function by generating secondary disease-causing mechanisms or pathways, such as: the generation of free radicals with subsequent damage to DNA, lipids, proteins and mitochondria; energy failure; aberrant intra-cellular signal transduction; cell membrane depolarization; apoptosis; activation of pro-inflammatory genes; the propagation of adverse feedback loops; and subsequent cell death.

10. There are a finite number of these secondary mechanistic pathways that comprise a cellular response to disease. A teaching of the Specification of the invention is that these common secondary pathways are implicated, in varying degrees, in any neurological insult or disease. This insight is an important component of the current invention. With this knowledge, active therapeutic agents may be formulated in accordance with the invention in appropriate combinations, amounts, and ratios to act therapeutically for all conditions of neurological impairment.

11. To maximize the therapeutic response in accordance with the invention, one skilled in the art administers a selected combination of nutrients specifically chosen based upon the clinical situation at hand. The selection of a combination of

Serial No. 09/837,562
Declaration Of Edward Larry McCleary
Page 3 of 7
187551v1

agents is influenced by the knowledge of the one skilled in the art (e.g., a physician), the specific disease processes involved, and the clinical condition of the patient.

12. Thus, there is a difference between the primary cause of any neurological insult producing impaired or deteriorating neurological function, and the finite universe of secondary processes that, in reality, constitute the final common pathways of nervous system dysfunction. The secondary insults need treatment as much as, if not more so, than the disease trigger itself. A combination of agents in accordance with the invention may also be given early in the course of any adverse condition in anticipation of its subsequent utility.

13. As outlined in the Background section of the Specification, functional neurological deterioration or dysfunction involves the development of concurrent aberrations in a network of complex mechanistic pathways of disease causation. These etio-patho-physiologic pathways contribute to neurological deterioration and/or dysfunction and are amenable to therapeutic intervention. Simply stated, pathway dysfunction produces neurological dysfunction.

14. The causes of different diseases are different. For example, the cause of brain cancer is different from the cause of a blood clot, which is different from the cause of multiple sclerosis. Nevertheless, the finite universe of mechanisms that are ultimately responsible for the production, or causation, of damage to nerve cells in the brain and central nervous system are common to substantially all disorders, the mechanisms being present in different relative proportions depending on the insulting stimulus or stimuli.

15. A method in accordance with the invention, as claimed in claims 24 and 59 – 64, treats the common mechanisms, or pathways, and thereby treats the impaired or deteriorating neurological function caused by an underlying disease process. Compositions and methods in accordance with the invention, however, do not necessarily or typically cure the underlying cause of the disease, for example, a cancer or blood clot.

16. One skilled in the art, for example, a physician, typically knows and

Serial No. 09/837,562

Declaration Of Edward Larry McCleary

Page 4 of 7

187551v1

recognizes one or several predominant mechanisms arising from a particular insulting stimulus of a particular disease process. For example, a neurosurgeon cares for a patient that might have a blood clot or a tumor in the brain. A neurologist might care for a patient with Alzheimer's disease or Lou Gehrig's disease. A neonatologist cares for a premature baby. Each of the specialists typically has a good idea of one or several predominant abnormal mechanisms associated with a particular disease or condition that underlies impaired or deteriorating neurological functions.

17. Teachings of the prior art, however, typically lack a comprehensive overview including all of the common mechanisms implicated in all neurological diseases. Therefore, a practitioner using the prior art lacks the knowledge and skills that would enable him to influence therapeutically more than one or a few of the various dysfunctional mechanisms.

18. An important teaching of the invention is that a relatively finite number of mechanisms, or pathways, are common to all impaired or deteriorating neurological functions.

19. As inventor of the invention, I systematically developed in a holistic fashion a nutritional supplement composition, as claimed in claims 1 and 53 – 58, and a method for treating, as claimed in claims 24 and 59 – 64.

20. Having analyzed disease-producing pathways to identify the loci of specific control mechanisms, their modulating factors, and rate-limiting steps, I developed a general therapeutic paradigm that enables one skilled in the art to treat any impaired or deteriorating neurological function. See the Specification, page 16, lines 29 – 31 and page 29, lines 3 – 6.

21. Using the teachings of the Specification, his knowledge and skills, and a method in accordance with claims 24 and 59 – 64, one skilled in the art is able to formulate a composition and administer it to a patient to treat suitably any impaired or deteriorating neurological function.

22. A method in accordance with claim 24 treats an impaired or deteriorating neurological function through the administration to a patient for a therapeutically

Serial No. 09/837,562

Declaration Of Edward Larry McCleary

Page 5 of 7

187551v1

effective period an effective amount of a composition comprising a plurality of agents that in combination provide multiple simultaneous avenues of intervention in multiple disease mechanisms or pathways.

23. The claimed invention produces beneficial effects at many sites in various dysfunctional pathways. The present invention not only improves symptomatology, but actually functions at various sites to produce metabolic and physiologic changes that alter, modulate, and improve or reverse the basic abnormalities responsible for the development of various neurological diseases.

24. The level of predictability in the field of treating neurological function is low in the sense that firstly, the efficacy of every treatment varies from patient to patient, and secondly, practitioners in the prior art typically limit their treatments to only one or several of the disease pathways of a particular disease condition, rather than treating numerous common pathways that cause impaired or deteriorating neurological function. As a result, the predictability of therapeutic outcome is hampered.

25. Using compositions and methods in accordance with the invention, one skilled in the art more likely treats many or all of the abnormal mechanisms, or pathways, by which a particular disease process affects neurological function, rather than treating only one or a few of the mechanisms commonly recognized and associated in the prior art with the particular disease. This improves predictability of therapeutic outcome.

26. It is clear that one skilled in the art can customize administration of a composition to a patient depending on various factors, including the disease treated, the particular agents used, the route of administration, and the condition and age of the patient. Nevertheless, only by applying a method in accordance with the invention is one skilled in the art able to select agents suitable for influencing therapeutically many or all of the common disease mechanisms identified in the Specification.

27. In view of the high level of skill in the art of neurological therapy, the discussion of components A – M at pages 15 – 25 of the Specification, the teaching of effective and preferred ranges of agents at pages 25 – 27, and methods of

Serial No. 09/837,562

Declaration Of Edward Larry McCleary

Page 6 of 7

187551v1

administering compositions at pages 27 and 28, one skilled in the art is able to practice the invention defined in claim 24 without significant experimentation. Choices of specific agents (and their amounts) within a particular category are affected by knowledge available to one skilled in the art, as shown by multiple examples in the Background section. This includes knowledge of the underlying disorder and the location and mechanism of action of specific therapeutic agents.

28. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001, and that such willful false statements may jeopardize the validity of the Application or any patent issued thereon.

10/28/03
Date

Edward Larry McCleary
Edward Larry McCleary

Serial No. 09/837,562
Declaration Of Edward Larry McCleary
Page 7 of 7
187551v1